Panprudent - D

Pantoprazole 40 mg + Domperidone 30 mg (SR) Capsules

1. **Generic Name:** Pantoprazole and Domperidone
2. **Qualitative and Quantitative composition**

Each hard gelatin capsule contains:

- Pantoprazole Sodium IP
- (Equivalent to Pantoprazole (as enteric coated tablets) 40 mg
- Domperiodone IP 30 mg
- (As prolonged release pellets)
- Excipients : (Approved colors used in hard gelatin capsule shell)

3. **Dosage form and strength**

Panprudent D is available in hard gelatin capsule containing Pantoprazole 40mg and Domperidone 30mg

4. **Clinical particulars**

4.1 Therapeutic indication

Combination of pantoprazole and domperidone is indicated for the treatment of Gastroesophageal reflux disease (GERD).

4.2 Posology and method of administration

One capsule once daily preferably before meal or as directed by the physician.

4.3 Contraindication

PANTOPRAZOLE Pantoprazole is contraindicated in patients with known hypersensitivity to any component of the formulation or any substituted benzimidazole. Hypersensitivity reactions may include anaphylaxis, anaphylactic shock, angioedema, bronchospasm, acute interstitial nephritis, acute kidney injury, and urticaria.

DOMPERIDONE Domperidone is contraindicated in the following situations: Known hypersensitivity to domperidone or any of the excipients. Prolactin-releasing pituitary tumour (prolactinoma.) Domperidone should not be used when stimulation of gastric motility could be harmful: gastrointestinal haemorrhage, mechanical obstruction or perforation.

4.4 Special warnings and precautions for use

PANTOPRAZOLE

Concurrent Gastric Malignancy Symptomatic response to therapy with Pantoprazole does not preclude the presence of gastric malignancy.

Atrophic Gastritis

Occasionally in gastric corpus biopsies from patients treated long-term with Pantoprazole, particularly in patients who were H. pylori positive.

Acute Interstitial Nephritis

Acute interstitial nephritis, acute kidney injury may occur at any point during PPI therapy and is generally attributed to an idiopathic hypersensitivity reaction. Discontinue pantoprazole if acute interstitial nephritis, acute kidney injury develops.

Cyanocobalamin (Vitamin B-12) Deficiency

Generally, daily treatment with any acid-suppressing medications over a long period of time (e.g., longer than 3 years) may lead to malabsorption of cyanocobalamin (Vitamin B-12) caused by hypo- or achlorhydria. Rare reports of cyanocobalamin deficiency occurring with acid- suppressing therapy have been reported.

Patients with Hepatic Impairment: Doses higher than 40 mg/day have not been studied in patients with hepatic impairment.

DOMPERIDONE

Use in liver disorders Since domperidone is highly metabolised in the liver, domperidone should be not be used in patients with hepatic impairment.

Renal insufficiency: In patients with severe renal insufficiency (serum creatinine > 6 mg/100 mL, i.e. > 0.6 mmol/L) the elimination half-life of domperidone was increased from 7.4 to 20.8 hours, but plasma drug levels were lower than in healthy volunteers. Since very little unchanged drug is excreted via the kidneys, it is unlikely that the dose of a single administration needs to be adjusted in patients with renal insufficiency. However, on repeated administration, the dosing frequency should be reduced to once or twice daily depending on the severity of the impairment, and the dose may need to be reduced. Such patients on prolonged therapy should be reviewed regularly.

Use with ketoconazole : A slight increase of QT interval (mean less than 10msec) was reported in a drug-drug interaction study with oral ketoconazole. Even if the significance of this study is not fully clear, alternative therapeutic options should be considered if antifungal treatment is required. There are limited post-marketing data on the use of domperidone in pregnant women. A study in rats has shown reproductive toxicity at a high, maternally toxic dose. The potential risk for humans is unknown. Therefore, domperidone should only be used during pregnancy when justified by the anticipated therapeutic benefit.

4.5 Drug interactions

PANTOPRAZOLE

Interference with Antiretroviral Therapy: Concomitant use of atazanavir or nelfinavir with proton pump inhibitors is not recommended. Coadministration of atazanavir or nelfinavir with proton pump inhibitors is expected to substantially decrease atazanavir or nelfinavir plasma concentrations and may result in a loss of therapeutic effect and development of drug resistance.

Coumarin Anticoagulants: There have been postmarketing reports of increased INR and prothrombin time in patients receiving proton pump inhibitors, including Pantoprazole, and warfarin concomitantly. Increases in INR and prothrombin time may lead to abnormal bleeding and even death. Patients treated with proton pump inhibitors and warfarin concomitantly should be monitored for increases in INR and prothrombin time.

Clopidogrel:Concomitant administration of pantoprazole and clopidogrel in healthy subjects had no clinically important effect on exposure to the active metabolite of clopidogrel or clopidogrel induced platelet inhibition. No dose adjustment of clopidogrel is necessary when administered with an approved dose of pantoprazole.

Drugs for Which Gastric pH can Affect Bioavailability Pantoprazole causes long-lasting inhibition of gastric acid secretion. Therefore, pantoprazole may interfere with absorption of drugs where gastric pH is an important determinant of their bioavailability (e.g., ketoconazole, ampicillin esters, and iron salts).

False Positive Urine Tests for THC There have been reports of false positive urine screening tests for tetrahydrocannabinol (THC) in patients receiving proton pump inhibitors. An alternative confirmatory method should be considered to verify positive results.

Methotrexate Concomitant administration of PPIs and methotrexate may elevate and prolong serum levels of methotrexate and/or its metabolite hydroxymethotrexate. However, no formal drug interaction studies of methotrexate with PPIs have been reported.

DOMPERIDONE

The results of this interaction study should be taken into account when prescribing domperidone concomitantly with strong CYP3A4 inhibitors: for example: ketoconazole, ritonavir and erythromycin.

4.6 Use in special population

PANTOPRAZOLE

Pediatric Use : The safety and effectiveness of pantoprazoe for short-term treatment (up to eight weeks) of erosive esophagitis (EE) associated with GERD have been reported in pediatric patients

Neonates to less than one year of age :The use of Pantoprazole for treatment of symptomatic GERD in infants less than 1 year of age is not indicated.

Geriatric Use: In short-term reported clinical trials, erosive esophagitis healing rates in the 107 elderly patients (≥ 65 years old) treated with Pantoprazole were similar to those found in patients under the age of 65. The incidence rates of adverse reactions and laboratory abnormalities in patients aged 65 years and older were similar to those associated with patients younger than 65 years of age

DOMPERIDONE

Use during lactation:The total amount of domperidone excreted in human breast milk is expected to be less than 7 micrograms per day at the highest recommended dosing regimen. It is not known whether this is harmful to the newborn. Therefore breast-feeding is not recommended for mothers who are taking domperidone.

Use in infants:

Neurological side effects are rare. Since metabolic functions and the blood-brain barrier are not fully developed in the first months of life the risk of neurological side effects is higher in young children. Therefore, it is recommended that the dose be determined accurately and followed strictly in children. Overdosing may cause extrapyramidal symptoms in children, but other causes should be taken into consideration

4.7 Effects on ability to drive and use machine

Adverse drug reactions, such as dizziness and visual disturbances may occur .If affected, patients should not drive or operate machines.

4.8 Undesirable effects

Immune system disorders

Very rare: Hypersensitivity reactions.

Psychiatric disorders

Very rare: Nervousness, somnolence, depersonalization.

Immune system disorders

Very rare: Tiredness-asthenia, lethargy, drowsiness, headache, vertigo, tremor, and paresthesia. An individual case of tonic-clonic convulsions and petit mal episode has been reported.

Eye diseases

Individual cases of mydriasis and of loss of the bilateral visual faculty have been reported. In both cases, the reactions resolved following the discontinuation of the drug.

Cardiac diseases
Very rare: Palpitation, tachycardia. An individual case of atrial bigeminy has been reported.

Vascular disorders
Very rare: Hypotension

Respiratory, thoracic and mediastinal disorders
Very rare: Dyspnea, cough, edema of the respiratory tract.

Gastrointestinal disorders
Very rare: Nausea, vomiting, heartburn and gastralgia, dyspepsia, and diarrhea. Two individual cases of glossitis and aphthous stomatitis have been reported. An individual case of cholestatic hepatitis and another case of hypoglycemic coma in an elderly patient receiving concomitant oral hypoglycemic agents have been observed.

Skin and subcutaneous tissue disorders
Very rare: Allergic skin eruption, urticaria, erythema, exanthema, itching, and angioedema. An individual case of epidermolysis with fatal outcome has been reported.

Musculoskeletal and connective tissue disorders
Very rare: Asthenia and weakness of lower extremities.

General disorders and administration site disorder
Very rare: Allergic and anaphylactoid reactions. General malaise. Individual cases of generalized edema, syncope, and asthenia have been rarely reported. An individual case of sleepiness, hypotonia and vomiting in a newborn has been reported after the administration of levodropropizine in the lactating mother. In this case, symptoms, which appeared after breastfeeding, spontaneously resolved after discontinuing breastfeeding.

4.9 Overdose

PANTOPRAZOLE
Experience in patients taking very high doses of pantoprazole (> 240 mg) is limited. Spontaneous post-marketing reports of overdose are generally within the known safety profile of pantoprazole. Pantoprazole is not removed by hemodialysis. In case of overdosage, treatment should be symptomatic and supportive. Single oral doses of pantoprazole at 709 mg/kg, 798 mg/kg, and 887 mg/kg were lethal to mice, rats, and dogs, respectively. The symptoms of acute toxicity were hypoactivity, ataxia, hunched sitting, limb-splay, lateral position, segregation, absence of ear reflex, and tremor.
DOMPERIDONE

Symptoms of overdosage may include drowsiness, disorientation and extrapyramidal reactions, especially in children.

Treatment: There is no specific antidote to domperidone, but in the event of overdose, gastric lavage as well as the administration of activated charcoal, may be useful. Close medical supervision and supportive therapy is recommended. Anticholinergic, anti-parkinson drugs may be helpful in controlling extrapyramidal reactions.

5. Pharmacological properties

5.1 Mechanism of action

PANTOPRAZOLE

Pantoprazole is a proton pump inhibitor (PPI) that suppresses the final step in gastric acid production by covalently binding to the H+/K+ -ATPase enzyme system at the secretory surface of the gastric parietal cell. This effect leads to inhibition of both basal and stimulated gastric acid secretion, irrespective of the stimulus.

5.2 Pharmacodynamic properties

PANTOPRAZOLE

Pantoprazole is a proton pump inhibitor (PPI) that suppresses the final step in gastric acid production by covalently binding to the H+/K+ -ATPase enzyme system at the secretory surface of the gastric parietal cell. This effect leads to inhibition of both basal and stimulated gastric acid secretion, irrespective of the stimulus. It has been reported that the binding to the H+/K+ -ATPase results in a duration of antisecretory effect that persists longer than 24 hours for all doses tested (20 mg to 120 mg).

DOMPERIDONE

Domperidone is a dopamine antagonist with anti-emetic properties. Domperidone does not readily cross the blood brain barrier. In domperidone users, especially in adults, extrapyramidal side effects are very rare, but domperidone promotes the release of prolactin from the pituitary. Its anti-emetic effect may be due to a combination of peripheral (gastrokinetic) effects and antagonism of dopamine receptors in the chemoreceptor trigger zone, which lies outside the blood-brain barrier in the area postrema.. There is no effect on gastric secretion

5.3 Pharmacokinetic properties

PANTOPRAZOLE

This drug acts to decrease gastric acid secretion, which reduces stomach acidity.

Absorption: After administration of a single or multiple oral 40 mg doses of Pantoprazole, the peak plasma concentration of pantoprazole was achieved in approximately 2.5 hours. Pantoprazole undergoes little first-pass metabolism, resulting in an absolute bioavailability of approximately 77%. Pantoprazole absorption is not affected by concomitant administration of antacids. Administration of Pantoprazole Tablets with food may delay its absorption up to 2 hours or longer.Thus, Pantoprazole may be taken without regard to timing of meals**.**

Metabolism: Pantoprazole is metabolized in the liver by the cytochrome system.

Elimination: After hepatic metabolism, almost 80% of an oral or intravenous dose is excreted as metabolites in urine; the remainder is found in feces.

Half-life
About 1 hour

DOMPERIDONE
Domperidone is a dopamine antagonist with anti-emetic properties. Domperidone does not readily cross the blood brain barrier

- **Absorption:** Peak levels of domperidone following an oral dose occur after about 60 minutes.
- Plasma protein binding:
- **Metabolism:** Domperidone is metabolized in the liver and intestines with oral administration
- **Elimination:** Domperidone is eliminated 31% in urine and 66% in feces.

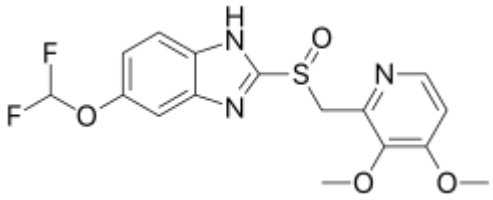
6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

Not required.

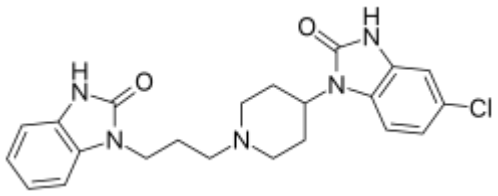
7. Description

- **Pantoprazole** belongs to class of medicines called proton-pump inhibitors. Its chemical name is(*RS*)-6-(Difluoromethoxy)-2-[(3,4-dimethoxypyridin-2-yl)methylsulfinyl]-1*H*-benzo[d]imidazole



Molar mass :383.37 g·mol^{-1}

- **Domperidone** is a D2 receptor antagonist. Its chemical name is 5-Chloro-1-(1-[3-(2-oxo-2,3-dihydro-1*H*-benzo[*d*]imidazol-1-yl)propyl]piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one



Molar mass: 425.92 g·mol−1

8. Pharmaceutical particulars

8.1 Incompatibilities

There are no known incompatibilities.

8.2 Shelf-life

24 Months

8.3 Packaging Information

Panprudent D is available in a strip

8.4 Storage and handling instructions

Store in cool and dry place.

9. Patient Counselling Information

9.1 Adverse Reactions

Refer part 4.8

9.2 Drug Interactions

Refer part 4.5

9.3 Dosage

Refer part 4.2

9.4 Storage

Refer part 8.4

9.5 Risk Factors

Refer part 4.4

9.6 Self-monitoring Information

NA

9.7 Information on when to contact a health care provider or seek emergency help

Patient is advised to be alert for the emergence or worsening of the adverse reactions and contact the prescribing physician.

9.8 Contraindications

Refer part 4.3

10. Manufactured by RAVENBHEL HEALTHCARE PVT

11. Details of permission or licence number with date : 10/12/24

JK/01/56 and JK/01/57

12. Date of revision : April 2025